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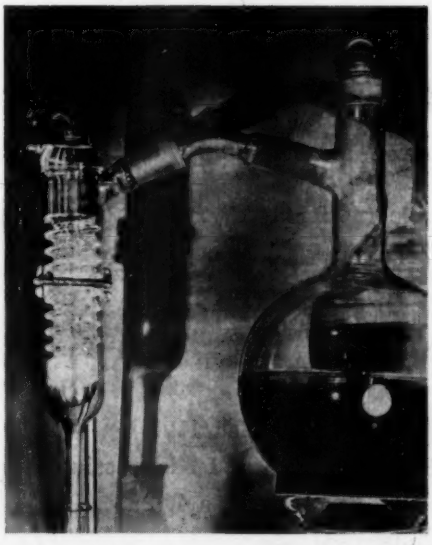

PREPARATION OF REDISTILLED
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Since 1825 *August 1946*

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AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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CONTENTS

HOSPITAL PHARMACY

NO branch of pharmacy has shown such rapid growth in importance and prestige during the past few years as has hospital pharmacy. At one time the hospital pharmacist, in the present understanding of the term, was a rarity. In many hospitals the so-called pharmacy was essentially a storeroom and the dispensing of drugs was performed by nurses or internes and, in some instances, by persons totally without technical or professional training. This condition has and is changing rapidly. Today a hospital pharmacist is more than a clerk handing out drugs and supplies upon order. In the large and growing number of good hospital pharmacies the manufacture of many drug products has become routine practice with a considerable saving resulting. Many institutions now entrust their pharmacy department with the preparation of parenteral solutions which is a task requiring considerable professional training and skill. The real province, however through which the hospital pharmacist has gained most in recognition and prestige is in his service as a source of information for the medical staff on new therapy. The advances in newer therapeutics have been so rapid that only a specialist in this field can hope to keep abreast of the constant stream of new developments that literally pour from the research laboratories of the drug industry. Most physicians have long since despaired of keeping pace with these new substances but yet they realize the importance of adopting them if they are to give their patients the benefit of the most effective therapy. When they find a pharmacist in whom they can have confidence and who can tell them the drug of choice for a given condition, its indications, contra-indications, dosage, mode of administration, cost, and all other pertinent data they are then and there boosters for pharmacy of the first magnitude. There are hospital pharmacists who have developed such a reputation in giving this advice that a major part of their time is spent in giving information and guidance to the physician, time well spent both from the standpoint of our relations with the medical profession as well as from the standpoint of improving medical care. The truth is that one really good hospital pharmacist does more to improve physician-pharmacist relations than ten interprofessional relations committees organized with the objec-

tive of trying to draw these groups together with arguments as to why it should be so.

This increased importance of hospital pharmacy carries with it serious responsibilities since a poor pharmacist in the hospital exercises just as great a negative value as does the good one a positive. Pharmaceutical educators are aware of this fact and already plans are being made to give special attention to the training of hospital pharmacists over and beyond that training now given in the regular four year pharmacy course. Evidence of such a trend is seen in the paper by Dr. Glenn L. Jenkins, of Purdue University, retiring president of the American Association of Colleges of Pharmacy, read before the American Society of Hospital Pharmacists and entitled "Educational Requirements for a Pharmacist from the Viewpoint of an Educator".

There is no doubt but that the duties and opportunities afforded the hospital pharmacist call for a superior type of training. Many believe it should be on a graduate level with internship in the hospital a final requirement. Now is the time to raise the standards for training these most essential pharmaceutical specialists. Pharmacy should not fail to meet this challenge. Never has there been a greater opportunity to advance the cause of pharmacy and to raise its professional prestige in a sound and enduring manner.

L. F. Tice.

THE EFFECT OF ACETONE ON THE SURFACE TENSION AND THE BACTERICIDAL EFFICIENCY OF AEROSOL OT

By Louis Gershenfeld and Saul M. Shulik*

Introduction

THERE are several prominent theories as to the action of disinfectants in the destruction or inhibition of bacterial growth. The first theory that was postulated, by Henle in 1889 (1), considered the bactericidal action as being due to a chemical reaction that occurred between the disinfectant and the bacterial cell. Several years later in 1891 Abbott (2) advanced his "biological" theory which maintained that the time required for the killing of bacteria by a disinfectant is directly proportional to the resistance of that organism. Thus, bacteria of equal resistance would die simultaneously upon the action of a bactericide. The third theory which is called the "modern" theory is advocated in preference to the above. Embodied in this theory is the idea that "the bactericidal action of a bactericide is due to its diffusion through the cell wall" of the bacteria (3). Investigation has shown that the diffusibility of a disinfectant through this membrane is a function of certain physical phenomena among which surface tension plays an important role (4).

Surface tension may be defined as "the pull in dynes exerted on either side of an imaginary line one centimeter long lying within the liquid surface" (5). Frobisher sums up the action of surface tension in disinfection in the following four points (6):

1. The low surface tension of a solution permits it to better penetrate small cracks and crevices.

2. The lowering of the surface tension will increase the rate of osmosis and diffusion of a solution.

3. Adsorption of disinfectants that lower the surface tension occurs at the surface of the organism and, consequently, there is a greater concentration of the toxic agent where it will do the most good.

* Department of Bacteriology, Philadelphia College of Pharmacy and Science.

4. Temperature influences the adsorption of surface tension reducents; the lower the temperature, the greater the amount of reducent adsorbed.

"It has been shown by du Nouy that the surface tension of a solution which contains surface tension reducents becomes continuously lower on exposure to air" (6) due to the accumulation of the molecules of the reducent at the surface during the time of the experiment. Consequently, the rapidity of making surface tension measurements is essential for accurate results. The actual measurements of the surface tension can be made with the du Nouy tensiometer which measures the pull on a platinum ring of the surface of the test liquid. "The pull is transmitted through a lever fixed at right angles to a twisted steel wire, the torsion of which is registered on a dial" (6).

Not only the disinfectant but also the depressant may exhibit bactericidal action. As Gershenfeld and Perlstein (7) pointed out, the depressant may be bactericidal according to the following: When the depressant is added to a liquid, the molecules of the latter will have a stronger attraction for each other than for the molecules of the depressant. As a result the depressant will tend to be forced out of the liquid and accumulate at the interface between the liquid and the bacteria. Thus, it is conceivable that a concentration of the depressant will occur at the interface which will be toxic although its concentration in the body of the liquid may not be so. This adsorption of the reducent or depressant interferes with the diffusion of the nutrient material into these organisms and causes their starvation (6).

Hydrogen-ion concentration is another important factor in the action of bactericides. It has been shown that Aerosol OT "exerts *in vitro* a marked increase in bactericidal efficiency with an increase in hydrogen-ion concentration. It is therefore important especially in the case of solutions of Aerosol OT, to note or approximate the pH of the final mixture if a bactericidal effect is desired" (12).

Naturally, the more concentrated the disinfectant (Aerosol OT) the greater will be its efficiency (12). A good disinfectant is one which shows bactericidal properties at relatively low concentrations.

The purpose of this investigation was to determine the effect of surface tension on the bactericidal activity of Aerosol OT when a constant pH of 6.5 was maintained throughout the entire experiment.

Procedure

As was previously pointed out above, the concentration and pH of an Aerosol OT solution markedly affect its action in respect to killing bacteria. Therefore, these two factors were kept at constant values throughout the experiment. A 1:3000 Aerosol OT solution was used and maintained at a pH of 6.5. This pH was chosen because it has been proven that a 1:3000 Aerosol OT solution is not bactericidal at that pH (12) (see Table II).

TABLE I

pH of the final mixture	7.0		6.8		6.6		6.4	
Time in min.	5	10	5	10	5	10	5	10
Dilutions								
1:2000	+	+	+	+	—	—	—	—
1:3000	+	+	+	+	+	+	+	—
1:4000	+	+	+	+	+	+	+	+

Acetone was used to change the surface tension of the solution of Aerosol OT. Prior to its use, its bactericidal activity had to be determined. Phenol Coefficient tests revealed the maximum concentration of acetone that did not kill in fifteen minutes. Because of the low surface tension of acetone, a four mm. loop would not hold a drop of the latter, and a modified Phenol Coefficient technique had to be employed. Instead of using a loop, 1 cc. pipettes were substituted and 0.1 cc. of the mixtures was transferred to the F. D. A. broth. The results are recorded in Table II:

TABLE II

RESULTS ON THE BACTERICIDAL ACTIVITY OF ACETONE

% Acetone	100%	60%	55%	50%	45%	40%	35%	30%	25%
5 minutes	—	—	—	+	+	+	+	+	+
10 minutes	—	—	—	—	—	+	+	+	+
15 minutes	—	—	—	—	—	+	+	+	+

In the above tests *Staphylococcus aureus* was the test organism and the temperature was 37° C. Aside from the slight modification mentioned, the technique was as designated in the F. D. A. Phenol Coefficient Test (11).

All solutions in the experiment were adjusted to a pH of 6.5 and no change in pH was noted when checked at the end of the experiment. In the case of the Aerosol OT solutions, various difficulties were encountered when using the colorimetric method. This necessitated the use of the electrometric method for determining the pH. It might be of interest to note that the following occurred when attempting to determine the pH of Aerosol OT solutions colorimetrically: If twenty drops of base were added a drop at a time with shaking, an acid pH resulted; but when the twenty drops of base were added at one time the solution became alkaline. Also, there seemed to be a reaction between the indicator (bromothymol blue) and the Aerosol OT because the color of the indicator changed upon standing for a brief period of time.

In order to have the acetone concentration as the only variable in the acetone-Aerosol OT solutions, the following method of preparation was employed:

Preparation of Solutions

Stock solution of Aerosol OT—1 Gm. Aerosol OT 100% in distilled water q. s. to 100 cc. equals a 1:100 solution of Aerosol OT. The Aerosol OT pellets were soaked in water for twenty-four hours and then the solution was autoclaved.

Solution A—prepared just before test—2 cc. stock solution were mixed aseptically with 58 cc. sterile distilled water forming a 1:3000 Aerosol OT solution.

Solution B—prepared just before test—3 cc. of stock solution were mixed aseptically with 42 cc. of sterile distilled water plus 45 cc. of acetone forming a 1:3000 Aerosol OT in a 50% acetone solution.

Test Solution	Solution A	Solution B	% Acetone in Solutions
a	1 cc.	9 cc.	45%
b	2 cc.	8 cc.	40%
c	3 cc.	7 cc.	35%
d	4 cc.	6 cc.	30%
e	5 cc.	5 cc.	25%
f	6 cc.	4 cc.	20%
g	7 cc.	3 cc.	15%
h	8 cc.	2 cc.	10%

A standard F. D. A. Phenol Coefficient Test was conducted on the above test solutions with *Staphylococcus aureus* at 37° C. The results are found in Table III:

TABLE III

RESULTS OF MANY TESTS REVEALING THE BACTERICIDAL ACTIVITY OF 1:3000 AEROSOL OT WITH VARYING CONCENTRATIONS OF ACETONE

% Acetone	45%	40%	35%	30%	25%	20%	15%	10%
5 minutes	—	—	—	+	+	+	+	+
10 minutes	—	—	—	—	+	+	+	+
15 minutes	—	—	—	—	+	+	+	+

Resistance of test organism—a 1:90 Phenol killed in 10 min. All controls were satisfactory.

Surface tension measurements were made on the test solutions with the du Nouy tensiometer. The following are the results of several measurements of the same solutions, each of which was exposed to the air for a period of one minute:

TABLE IV

SURFACE TENSION MEASUREMENTS

Test Solution	Dynes
a	38.22
b	39.93
c	40.91
d	41.40
e	41.77
f	41.65
g	41.65
h	41.16
A	39.20
B	37.24

Discussion

It will be noted from the foregoing experimental data that the surface tension of a 1:3000 Aerosol OT solution (Solution A) is

lower than that of all the test solutions except (a) (see Table IV). However, test solutions (b) and (c), with slightly increased surface tensions, were bactericidal whereas a 1:3000 Aerosol OT was not. Accordingly, it may be assumed that the bactericidal efficiency of an Aerosol OT solution is not dependent solely on its low surface tension.

A possible explanation of the lack of growth in test solutions (b) and (c) can be attributed to the previously mentioned theory suggested by Gershenfeld and Perlstein (7). Presumably, when a non-bactericidal concentration of acetone was added to the 1:3000 Aerosol OT solution, the former was forced out of solution because the molecules of Aerosol OT probably had a stronger affinity or attraction for each other than for the molecules of acetone. Thus, there accumulated at the interface between the bacteria and the solution a concentration of acetone which was much higher than that in the bulk of the test solution. This increased concentration of the acetone about the bacteria was responsible for the toxic effect displayed by solutions (b) and (c).

The reason for growth in test solutions (d) to (h) inclusive may be ascribed to the same theory advocated in the previous paragraph. Evidently the concentration of the acetone in these test solutions was not great enough to affect appreciably the concentration of the acetone at the bacteria-solution interface. Consequently, the concentration of acetone at this latter point was not of toxic proportions.

Summary

The non-bactericidal concentrations of an aqueous acetone solution were determined by the F. D. A. Phenol Coefficient technique (slightly modified). A 1:100 aqueous Aerosol OT solution was prepared from 100% Aerosol OT and sterilized in the autoclave for twenty minutes at fifteen pounds pressure (121° C.); its pH was adjusted electrometrically to 6.5. The 100% acetone and sterile distilled water were adjusted colorimetrically to a pH of 6.5. A 1:3000 aqueous solution of Aerosol OT and a 1:3000 Aerosol OT in a 50% acetone solution were prepared just before the test was conducted. Using these two stock solutions various acetone-Aerosol OT test solutions were prepared containing varying concentrations of acetone ranging from 10% to 45% by volume. F. D. A. Phenol Coefficient Tests were conducted on these test solutions and their surface tensions were determined using the du Nouy tensiometer.

Conclusions

Accepting the results of various workers and tests conducted by ourselves that a 1:3000 aqueous Aerosol OT solution at a pH of 6.5 is non-bactericidal (12), the following conclusions were drawn by the authors:

1. Solutions containing 1:3000 Aerosol OT in water and 35% or more by volume of acetone are bactericidal within five minutes against *Staphylococcus aureus* at a pH of 6.5.

2. Solutions of identical Aerosol OT content but of 30% acetone concentration are non-bactericidal within five minutes.

3. The surface tension of a 1:3000 aqueous Aerosol OT solution is increased on the addition of acetone up to a concentration of 40%.

4. The bactericidal efficiency of a 1:3000 aqueous Aerosol OT solution appears to be independent of its surface tension.

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MEDICAL PROBLEMS OF TODAY*

By R. P. Vivian, M. D.**

A FEW years ago such a title might have been used to introduce a plea that vaccines, serums, or chemical substances be developed for therapeutic use in overcoming a variety of man's diseases. At this time much has been done to bring many diseases under control. We have learned how to avoid some, and we are able to prevent a few.

Today's title might well be used to focus attention upon the need for discovering a cure for cancer, or tuberculosis, or infantile paralysis. Such cures are definitely needed, but they are not the most urgent problems. Our present knowledge of medical science has given us for the first time in history the opportunity to obtain an ascendency over disease. The fullest use of our present resources can go far in limiting fatalities and disability. There is much that we can do in the way of arresting disease while awaiting the development of more specific treatment. The most urgent medical problem of today is how to apply our present knowledge of medical science for the benefit of a greater number of people.

May I remind you that the practice of medicine is defined as the science and art concerned with the cure, alleviation or prevention of disease, and with the restoration and preservation of health. The immediate problem might be simplified into how to establish the personnel and facilities for good health services, how to obtain these services economically, and to teach people how to use them.

Curative medicine has been foremost in everyone's mind. This is quite natural as it is the life-saving service for the afflicted. The conquests over disease have been spectacular. Pathological processes have become more accurately understood. The causative agents of many diseases have been found. Many therapeutic substances and procedures have been satisfactorily developed. The medical profession is very appreciative of the important contributions which the Pharmaceutical Manufacturers have made in this progress. I hope that the general public is also prepared to give credit to your really mag-

* Presented at the meeting of the American Pharmaceutical Manufacturers' Association, June 10, 1946.

** Strathcona Professor of Health and Social Medicine, McGill University.

nificent accomplishments. The conquests are spectacular, but they are frequently of only individual benefit. They are often beyond the reach of the many who know of, and desire to obtain, similar benefits.

Through our better understanding of disease we have acquired a limited knowledge of its prevention. Over the years there has been built up a public service in hygiene and preventive medicine. The basic program in public health is an old story. Communicable disease control and sanitation were its primary principles. Additions to the program have gradually been made. The steps taken in hygiene and preventive medicine for groups of people as in communities have been reasonably successful. This service should be generally extended. Further additions to the program are definitely required.

A growing interest in preventive medicine by more of the general public should now make it possible to further develop this field.

The more equal distribution of facilities, the presence of competent, well-trained personnel, ready to use their knowledge and possessing the means to do so could bring to a greater number of people in their own communities the advances in the practice of medicine.

One part of the medical problem of today is, therefore, how to supply the services that are needed, that will be used, that will be appreciated, and that can be paid for in one way or another. This has become a matter of general interest. People everywhere are deeply concerned about illness and its cost. It is being emphasized in public discussion. Responsible governments are attempting to meet the public demand through legislation and to provide the necessary money.

Caution is required.

One of the dangers of a period like the present when progress in social thought and development is enormously accelerated is a general tendency to exaggerate the importance of speed. People are so afraid of missing the bus that they tend to leap aboard without making sure of its destination and without even being certain that all their necessary luggage is with them.

The danger lies in the adoption of insufficiently considered plans with all their implications. The danger is real as regards both service and cost. As an illustration, I refer to the reportedly unhappy experience in New Zealand with its system of Health Insurance. Articles now appearing, which I have not seen denied, are stating that the service, as it exists, is far from complete in character or extent, that

the cost is bearing very heavily upon the taxpayers, and that the reputation of the medical profession has been seriously impaired.

In using this illustration I do not wish to belittle in any way the attempt of New Zealand to find an answer to some of the most pressing and perplexing problems in the practice of medicine. Nor do I deny the need for tax-obtained money to support good health services.

There is also danger in believing that a type of medical practice successful in some other country or even in another area of the same country may be generally applied with equal success.

In estimating the value of any health plan we must consider the character and knowledge of the people in the area, the type of service previously in effect, the medical standards of personnel and facilities, and the reliability of the statistics. We do know of tax-based programs that are successful both as regards service and cost. The success of these plans, in my opinion, can be directly attributed to the character of the people and their knowledge in matters of health. I am, however, inclined to believe that one of the plans most persistently advertised as successful in a country lacking freedom of speech, freedom of the press, and freedom of unbiased investigation is little more than the rosy-hued story of the setting up of something where nothing previously existed.

The interest of the public lies mainly in how to obtain curative services at less cost to the individual.

On this continent there are successful tax-based medical care programs of limited character that suit the region for which they were designed. Additions to these programs would improve the scope and quality of the service. The whole could provide the maximum possible for the areas concerned. In certain localities this system should prove to be excellent. If such a plan were wholly transplanted, it might suffer the fate of so many transplants—death from inanition in foreign soil because the ingredients for success were lacking in the new surroundings.

A tax-supported plan for medical care presents many problems. In my opinion, it must be sufficiently flexible to be adaptable to the varying conditions encountered. It must maintain the highest standards in medicine. It must not place an undue burden upon the taxpayer who is able to maintain a good state of health. It can only be effective if all the services that are required are adequately coordinated. The practice of medicine is really dependent upon the

fullest development which can be made in each of its component parts. These are not only curative medicine, hygiene and prevention, but also the broad field of social welfare. Social welfare is not merely the doling out of charity under another name from the taxpayers' pocket. It should be the means of attaining further advances in the progress of society as a whole. It can aid substantially in the program for man's betterment. We have seen for some time a growing interest in social welfare that belies the traditional statement of man's inhumanity to man. It began as so many worth while things have begun, through voluntary organization. It is now officially recognized as a responsibility of government by means of legislation and the allocation of tax money for this service. Many of the gaps that need to be filled in the services of curative medicine and public health could be aided by developments in the field of social welfare.

The medical problem of today may, therefore, be simply expressed by saying that it represents the need for the fullest development of all of the branches of medicine and their effective co-ordination to achieve the objective as defined. Each branch of curative medicine, public health, and social welfare, has a definite part to play. Each is dependent upon the other for the fullest development in its own field. All are dependent upon the provision of money, frequently from tax-collected funds. The provision of money for the payment of health services comprises the subject of Medical Economics. There is nothing mysterious about the subject of Medical Economics except the failure of some otherwise well-informed people to understand that the practice of medicine costs money, in fairly substantial amounts. Many people are today alive and reasonably well because of the advances of medical science which are justifiably costly in application. The lowering of medical standards or a reduction of service because of the cost is poor medicine and bad economics. This cost is, however, frequently more than the ordinary individual's pocket-book can meet without seriously affecting the family budget. Adequate medical care is sometimes foregone because of the economic barrier of cost to the individual.

Medical economics cannot be considered as an isolated subject. It must be thought of in relation to the entire economy of the local community and of the state. The provision of vast sums of money for health from tax sources is one thing. Its provision in relation to the economy of the state is quite another. The wise provision of

suitable sums and their careful expenditure in relation to value received should certainly be the objective.

These services cannot be provided solely on a treasury-minded basis, namely, a cash surplus. Neither can we jeopardize the entire economy of a country by providing, for purposes of political expediency, an ineffectual program at great cost. The need to do something, however, is urgent. Much could be done by adapting our present resources. The adaptation of our facilities and the training of personnel can only be achieved if we expand our interpretation of the practice of medicine. For obvious reasons we have been concentrating upon what we could do for disease as an entity. Man, however, is not something set apart. He belongs to a family, or a group, or a community. In treating man's diseases we must, therefore, consider man as a social being and take into account those factors in society which play an important part in his well-being. The practice of medicine must consider more than what it has learned through pathology and bacteriology. The applied sciences of physiology and biochemistry must be given greater opportunity. The social sciences must be taken into greater account. The future practice of medicine will be greatly benefited by what it can learn from a study of sociology in relation to medicine. In this way we can achieve a more effective co-ordination of all the services which go to make up the practice of medicine. Such thought has given rise to the development of a new branch of medicine, a branch which concerns itself with the study of the social factors that influence the attainment and maintenance of health. This new branch, social medicine, is as much a part of medicine as any other designated branch. It should not be confused with so-called socialized health services. Social medicine may be new as a subject but it is not new as an interest. Its emergence as an entity is simply a recognition of an aspect of medicine that needs to be developed. Its task is to show the way as to how all the services in the practice of medicine can be developed and co-ordinated in relation to society. We have limited examples of the effectiveness of some co-ordination. The story of tuberculosis is one. In Canada tuberculosis is now 7th in the 10 leading causes of death. In 1933 it was 4th. The reduction in the incidence of this disease has been achieved by the establishment of facilities and the presence of competent and well-trained personnel, methods of case-finding and treatment, and financial support from voluntary contribu-

tion and government grants. The whole has been brought about through education of the public.

The facilities have not only been established, but the medical profession has been trained, and wherever the public has been taught to utilize this service, a remarkable reduction in the incidence of tuberculosis has occurred. This, however, is only one field. It would be my hope that similar satisfactory results could be obtained by adopting the same methods in connection with cancer. In Canada cancer is and has been for some time the second of the leading causes of death. There is no sign as yet of any reduction in the number of deaths from this malignancy and, indeed, it is expected that the number of deaths will increase still further. In the absence of a specific cure, we could do much in the prolonging and saving of lives through early diagnosis and early treatment, provided we had the facilities, the personnel and the money with which to undertake a soundly planned campaign.

My remarks have largely dealt with the cure and alleviation and prevention of disease. There is another major concern of the practice of medicine—the preservation of health. Health is not merely the absence of disease; it is defined as well being. Well being is a relative term. The degree of well being of more of our people must be increased if we are to attain a fuller realization of a positive state of health. The greatest single medical problem of today is how to promote a more positive state of health. It is the task of tomorrow for the practice of medicine to assist more people to achieve that active and joyous state of well being which is health. *I believe that this can only be done through an improvement in our methods of disseminating Health Education.* Leadership in this might well come from the public service in hygiene and preventive medicine. This service has undertaken the task of the prevention of disease for groups of people. In the past this has been limited to fairly large groups. A program in personal hygiene and preventive medicine for the individual should be planned for effective application by the family physician and the community nurse.

These are the problems that must be solved if we are to apply our present knowledge of medical science for the benefit of a greater number of people. The problem as a whole is an urgent one. Present day trends indicate the need for a sound solution. These trends in the conduct of medical practice are plainly visible for those who

choose to look. They are developing as an expansion of the public health service with an augmented program and in the payment for medical care in whole or in part from tax-collected funds. These trends could be dangerous or they could make possible the most glorious period in medical history.

The problems may appear to be difficult—they are, but they can be solved. I believe that they can be dealt with by the same principles that have previously proven successful, fact finding, investigation and demonstration.

Sesearch has been the key which has unlocked so many doors that stood in the way of medical progress. The achievements in smallpox, diphtheria, diabetes and pneumonia are outstanding examples. *Sharing in all the accomplishments are those who have made possible the therapeutic agents—the pharmaceutical manufacturers.* Chemotherapy and the use of antibiotics are saving the lives of untold members because of your endeavors.

The application of research, is not your only contribution, however, as so many of the advances have been possible through your financial assistance, in the earliest stages of investigation.

The scope of the practice of medicine is expanding. Our efforts on man's behalf will be enhanced by the application of newer methods in the medical treatment of man in his relation to society. We are progressing from the alleviation and cure of disease to the greater prevention of illness, the attainment and maintenance of health. There is need for research into the socio-economic problems if we are to be successful. Health service is an inclusive term. Good health services are those which will supply the requisites for present day needs. The medical profession has a most important part to play in the establishment of such services.

The profession of medicine is an ancient and honorable one. For the past two thousand years and more it has attempted to minister for the health of people in the light of the knowledge of the times. New times bring new ideas, new ideas bring new responsibilities. Medicine is now faced with a new challenge which the rank and file of the profession will readily accept—how to apply our present knowledge of medical science for the benefit of a greater number of people.

It is a challenge which can not be avoided. The trends of present day thought indicate that it cannot be dismissed. Those trends are such that they cannot be stopped by the waving of hands or by the

cries of the privileged in a wilderness of misery. The story of Canute attempting to halt the tide should not be forgotten.

The trends, however, can be guided; guided to achieve the objective desired by so many, with the maintenance of standards that mean so much, by the use of proven principles that seem to be acknowledged by so few. The alternative to a successful response to the challenge could well be chaos.

The solution to this problem lies in viewing it with an open mind, in undertaking the fact-finding and investigation so necessary in any problem, in carefully planning methods of solution, and in making use of demonstrations wherever they can be established.

The medical profession cannot do this alone. Its members can do much by further developing their own fields but there must be understanding and co-operation by the general public in which the leadership which can be given by an organization such as this, would be invaluable.

"MECHANISM VS. VITALISM"

By Saul Caspe

THE intellectual is still seeking to know whether a human being is merely a machine or intricately a demi-god. Is man an understandable analysable mechanism or must he remain an intrinsically mystic vitalism? The answer to the question, is the human race all mechanism, all vitalism or possibly a mixture of these two "isms," is yet to be determined. The solution of this problem will complete our comprehension of the physiological, psychological, and even sociological sciences, and it will demonstrate clearly to us how the processes of body and mind in each and several individuals operate. Because a complete answer is impossible at present, we should wisely inform ourselves of the progress made toward this answer.

A housewife will confidently defy contradiction in asserting that her husband is a simple machine whose heart is controlled by his stomach. Any salesman can blatantly denude the deified character of men by cajoling them with psychological tid-bits. Apparently, our age has absorbed and has used the new knowledge gained by scientific investigation for practical purposes. There is nothing more practical than a successful method of approaching and influencing others. In the more detached world of medical science, the method pursued has been to study human beings as physical and chemical mechanisms, wherein each organ is recognized for its role in the corporate human machine. In contrast, high-minded preachers still inculcate in the lowly the indeterminate spiritual character of man. These preachers and their followers even become robust in the appreciation of human mental capacities which according to them defy any analysis. Even less tangible is the spirit, consciousness, free will and intricate emotional patterns. What is there to explain this conglomerate confusion known as the human race. There are only a few experiments and many theories.

The theory of mechanism implies that human beings are mechanisms operating with machine like precision. The theory of vitalism implies that human beings because of their minds and nerve systems ubiquitously possess a consciousness, a soul and a free will. The recent experimental results of William Stanley indicating that viruses may not be living substances has again focused attention upon

the controversial theories "vitalism vs. mechanism." Is man a machine or is man a soul, a consciousness, a vitalism? Does man possess a free will or is he incapable of possessing a free will? Is man solely the product of physical and chemical reactions which determine the mechanization of his body and mind? Is it a truism that man is the food he eats, the air he breathes, the environment that encompasses him? These questions inspire thought and elicit doctrines. For example, the radical social theorists believe that, "It is not the consciousness of men that determines their existence but on the contrary, their social existence determines their consciousness."

Based upon the experimental work of Ivan Pavlov, it can be axiomatically stated at present that each mechanism exhibits vital properties, and conversely, each vitalism manifests some mechanistic attributes. Most people are acquainted with the simple physiological reaction of salivation or watering at the mouth that accompanies automatically the sight or odor of food. Pavlov in experimenting with dogs was able by associating redundantly the sound of a bell with the giving of food eventually to stimulate salivation by the use of the indifferent agent (the bell) alone. Three hundred lessons were required by the first generation of mice to associate feeding time with a ringing bell. The second generation required only 100 lessons. The fifth generation required five lessons. These simple experiments have elucidated instinct, as well as the conditioned reflex mechanism, and have demonstrated that conditioned reflexes are inherited.*

At M. I. T. a machine has been constructed which is an analogue of the human stimuli—response reflex mechanism. This machine can be trained to associative phenomena just as simply as animals. Hence, it follows that the very important instinct and reflex behavior is mechanistic.

The vitalists, J. S. Haldane and H. V. Neal, while cognizant of these important experiments, still believe that mechanism tells us little of human behavior, and for that reason they adorn vitalism as their interpretation of individuality in organism. They admit, of course, certain mechanistic aspects of individuality. J. B. S. Haldane, the English scientist, reviews in "Philosophy in Science" the attributes of each school of thought and makes two statements which clearly illustrate the turbulent state in which both antagonists are conjecturing with accumulative but non-specific data.

* These results have been questioned.

"There are many objections to crude vitalism. Very careful work has shown that within limits of experimental error whole organisms and their parts obey the same thermodynamic laws as dead matter."

"The field of vision is continuous not mosaic, as might be expected from the fact that it depends on the impulses coming to the occipital nerve through half million nerve fibres. Illusion is a fact about the mind quite as typical as true perception." Can true perception and illusion be explained by mechanists?

Vitalism or Mechanism,—which philosophy approximates the truth, the earnest protagonist inquires. To answer this question, man must investigate which philosophy is extensible and which is intractible. The answer will always be fleeting or transitory because it will be based upon the incomplete whole.

The answer will also depend upon which shade of thought appeals to you. Monistic and dualistic mechanists and vitalists are merely sample categories. In fact, there are as many theories as there are religions and sects, and there is always an abounding supply of warriors who willingly desecrate their energies into these disuniting channels. It is the nature of the philosopher to correlate and integrate a comprehensive picture from the disunited and contradictory differentiations. It will be my privilege to restate certain scientific concepts, and to produce a unified picture which will approximate the truth. The phrase, approximate the truth, is used deliberately, for matter in its ultimate nature is as incomprehensible as space and time, and of necessity explanations must bring us down to the inexplicable.

There are men who catapult their verve and their mental and physical faculties against any set of laws that would tend to mechanize them. Their pride, ego, prejudices or poetic sense, force them to descry against any mechanistic doctrine. There are other groups of men equally intelligent who delight in minimizing the importance of man, his ego, his will, or his conscious freedom. To these materialists, man is just so much watered stock and like all watered stock he is not even fit to burn. Man, contend some scientists, is a lot of water, some fat, a little protein and some mineral for spicing,—he is mechanized and regulated by hormones from within and by stimuli from without. Some of the great talents of our age are identified with

both these classes of men. The average man vacillates between the two warring factions. He abhors the idea of man-made or controlled Robots,—Robots startle him. The effects of the antedated story of the Golem and the play R. U. R. are literary points of reference. In the "Brave New World" by Aldous Huxley we are prepared for scientific standardization; Men of exactly standardized physical and mental capacity. What strange bedfellows we become under such controlled conditions,—similar emotions, reflexes, physical forces, and with "you cannot tell them apart," appellations. Yet, the experimental and realizable possibilities entrance us. However, human regimentation in our everyday world provokes us either with a stimulus for its eradication or with a sense of ennui. Aside from these plausible phantasies or phantasmagories we are confronted today with men who actually are leaders or followers; men who think, and men who do not. The leaders visualize, the others think as a reflex habit, as a well understood mechanism. We often observe men who act contrary to a predetermined conditioned reflex; who sacrifice much to act according to a vision, a sense preception, or an illusion. Can the mechanism be established for their actions? The mechanists believe it can. Needless to say, the vitalists do not so believe; they are the disbelievers. Even men who are trained under exactly identical environmental conditions exhibit widely different mental and physical activities. In Shakespeare's *Julius Caesar,* we are confronted with two intransigents; Brutus and Cassius arriving at identical conclusions by different mental processes. Says Anthony of Brutus:

> "This was the noblest Roman of them all:
> All the conspirators save he,
> Did what they did in envy of Caesar;
> He only, in a general honest thought
> And common good to all, made one of them.
> His life was gentle: and the elements
> So mixed in him that Nature might stand up
> And say to all the World 'This was a man!'"

Will we ever be able to differentiate these mechanisms? Compton suggests that while the laws of physics are not violated in living organisms life takes advantage of the uncertainty principle to make certain events more probable than they otherwise would have been. Other scientists have considered life, mind and the electrons as wave

systems and the principle of uncertainty has been applied to them. In contrast, H. V. Neal affirms that mechanism fails to explain the activity of the conscious mind. Is it possible, he asks, to believe that a material universe devoid of mind has produced a mind capable of judging mechanism? However, in answer to this query we may interpret much conscious thinking as instinctive and conditioned and therefore the result of well understood mechanism.

A. S. Sachs in a chapter, "The Material Conception of the World," demonstrates the inadequacy in the philosophies of Fichte, Kant and Hegel and the possibilities in the theory of monistic materialism. He states, "Spirit is nothing more than a higher form of matter." And in another place he postulates: "Why is there continuity of life (omnia viva ex ovo), and why are we unable to create living organisms in the chemical laboratory from ordinary matter? Why are our efforts futile to find the secret of this cell matter which is the genetic origin of all life? What are the real distinctions between the inorganic, the non-living, and organic or living."

Sachs believes that even though materialism has not answered these questions, it is not sufficient ground for totally rejecting its doctrines.

We with our narrow yard sticks and arbitrary rules often confuse instead of simplifying human experience. Fallible as all men are, we still delight in our obdurate attempt to proselytize the naive layman. But, there is excellent compensation in this world; for where scientists fail, poets and philosophers flourish. Rarely does the scientist direct his attention to these latter for he is too busy with the specificity of his problems and laws. It is often, however, that the poet has instinctively and the philosopher intuitively taken the larger view. The great poets have never accepted man's arbitrary differentiation between the living and the dead. To the poet all matter is living. Their symphonies of gaunt austere mountains, lowly valleys, and crumbling continuities of life have the essence of a unity that bodes good to man in his enterprise. Who can read Shelley's "Ode to the West Wind" with its

> "O wild West Wind, thou breath of Autumn's being,
> Thou, from whose unseen presence the leaves dead
> Are driven, like ghosts from an enchanter fleeing"

without feeling the consciousness, the life force in so-called inanimate matter. When we browse alone in the murmuring forests, the con-

tinuity of life in the larger sense impresses upon us. "Dust thou art to dust returneth," says Longfellow the poet. The philosopher says the equivalent of the poet but with more rumination.

The renowned Emerson says:

> "Man is a center for nature running out threads through everything fluid and solid, material and elemental. The earth rolls,—every clod and stone comes to the meridian; so every organ, function, acid crystal, grain of dust has its relation to the grain. The highest moments come to us as a charm of nature—The glitter of the star, the sureness of affinity, the veracity of angles. Each material thing has its celestial side, has its translation through humanity into the spiritual and necessary sphere where it plays a part as indestructible as any other. And, to these their ends all things continually ascend. The gases gather to the solid firmament; the chemic lump arrives at the plant and grows; arrives at the quadruped, and walks; arrives at the man and thinks. Shall we say that quartz mountains will pulverize into innumerable Werners, Von Buchs and Beaumonts, and the laboratory of the atmosphere holds in solution I know not what, Berzeliuses and Davys?"

What is life? When matter, exhibits at least these activities; metabolism, reproduction and internal adaptations to change in environment, it is biologically considered life. But why do we limit ourselves to only these three activities? Inanimate and serene matter often manifests one or more of these activities, but is still considered dead. Arborescent crystals grow, rocks are formed by process of crystallization and growth and they are continuously nourished by the elements necessary for their growth. Brownian movements of small particles in water, reproduction by multiple fission, and internal response of the atom structure to external stimuli are other ordinary phenomena observed in all matter. Then, let us say all matter lives, and by life, we mean matter which exhibits any activity possessed by the most complex life,—man; metabolism, reproduction, locomotion, respiration, stimuli response, growth and numerous others. Jacques Loeb, in his book *Regeneration,* makes this interesting statement:

> "Living organisms, as well as crystals, are characterized by definite shape which is determined by the chemical nature of their

material. Both types of form grow, but the mechanism of growth is different in each."

Certain inanimate forms, such as charcoal and platinum, will absorb gases in one form and yield them in another form, and the process of making atomic from molecular hydrogen has been accomplished by this process of respiration. The behavior of electrons in our external world exhibits some of the most fascinating life-like properties. It is a little more difficult to accept this opinion of life than it is to accept the theory that plants live. Even among some people today plants are not considered alive. The acceptance of all matter as life of varying degrees of activity gives a continuity to all life which the previous hard lines of differentiation obstructed.

It is time for us to revise our rusty and musty notions, and banish with them our former religions and dogmas. With this new unified picture of life pervading everywhere the harsh and cold materialism vanishes and real continuity understood by all men replaces it. To build higher forms of mechanism of life activity from lower forms of life activity will then become an important step in the understanding of the oneness of life. Materialistic doctrine is a misnomer, and certainly H. V. Neal, if he accepts the notion of life herein proclaimed, as against the former arbitrariness, will admit the possibility of constructing mind from the material (life matter). The quibbling and disagreements of vitalists and mechanists will be wiped out because they were arguing on false premises, i. e. that there exist two states of matter: the living and non-living.

The men with the instinct of the cougar on the scent will track down the incongruities of life and analyze them and even synthesize them. Let us stop debating about terminology and arbitrary and oft harsh differentiation and direct these spent energies with a fortuitous will in raising man to a level of knowledge which is his heritage.

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ARTIFICIAL DISINTEGRATION OF ATOMS

A Historical Survey of Nuclear Fission*

Editor's Note—The following article taken from the "Pharmaceutical Journal" is one of the most easily understandable presentations that has appeared on this subject. It is, therefore, reprinted herewith for the benefit of our readers.

THE discovery of the fission of uranium and its application in the atomic bomb is no isolated event, but follows a series of discoveries which, since the end of last century, have been the basis of the modern science of physics. Classical ideas on the nature and properties of matter culminated in the atomic theory of the nineteenth century. The fundamental break occurred when Becquerel, in 1896, discovered that uranium was continuously emitting radiation of an unknown type which could penetrate matter and affected a photographic plate. Part of this radiation, the so-called "*alpha* rays," consists of helium atoms, carrying a positive charge of electricity, and these were found to be of the greatest value as a tool for further exploration of the structure of atoms.

It was, in fact, research on the penetration of matter by "*alpha* rays" which led Rutherford in 1911 to the fundamental discovery that the whole mass of each atom was concentrated in a minute central nucleus which carried a positive electric charge. Round this minute central nucleus, but at relatively great distances, revolved elementary negative electric charges—the "electrons"—in numbers sufficient to neutralize exactly the positive charge of the nucleus. The mass of these electrons was negligible compared with that of the nucleus. Niels Bohr, of Copenhagen, put forward a theory in 1913 which combined Rutherford's model of the "nuclear atom" with the quantum theory of energy enunciated by Planck to explain limitations of the classical electro-magnetic theory. It was immediately understood that any element, with a given charge on the nucleus, could exist in more than one modification with different atomic masses but almost identical physical and chemical properties.

* Reprinted from the *Pharmaceutical Journal.*

Work on the Isotopes

The existence of such modifications, "isotopes," of any element had first been suggested by Soddy in 1910. Aston, at Cambridge, followed up work, which had been started by J. J. Thomson, and proved that the great majority of elements consisted of a mixture of two or more isotopes and that the relative weight of the atom of any given isotope of any element was very nearly a simple multiple of the weight of a hydrogen nucleus, or proton. In 1932 Urey and Brickwedde showed that hydrogen itself is not a simple element, but contains a small amount (about 1/5000) of an isotope known as "heavy hydrogen" or deuterium, which has almost double the mass of a proton. Because, in this case, the ratio of the masses of the isotopes is as two to one the physical and chemical properties of hydrogen and deuterium are sensibly different, and it was found possible to separate them, in a pure state, in large amounts by normal technical methods.

The first decisive step in the solution of the problem was taken by Rutherford who, in 1919, showed experimentally that the charged *alpha* particles from radium-C could, in rare instances, collide with the nucleus of an atom of the common element nitrogen in such a way that it broke up and, as a result of the collision, the nuclei of two other atomic species or elements (oxygen and hydrogen) were formed.

A further very important step was taken in 1932 when Cockroft and Walton carried out an experiment in which hydrogen nuclei, produced artificially in an electric discharge and accelerated to a high velocity by means of an applied voltage, were used to bombard another stable element, lithium. The atoms of this element were found to disintegrate, and transmutation had been achieved in a completely controlled laboratory experiment. In this transmutation, and in others which followed this new discovery, the release of energy was enormous for such a minute event as a reaction involving a single nucleus. Nevertheless, the number of nuclear reactions was so small that the amount of energy generated by the reaction was extremely small compared with the total input of energy used to produce the bombarding particles. The practical value of these reactions as a source of energy was still completely negligible.

The reason is not far to seek; not only are these nuclear reactions very rare events, but the reactions are not self-propagating.

This is quite different from the chemical reactions with which we are familiar in our daily life; in nuclear reactions the particles emitted are of the same kind that initiated them and in sufficient numbers to affect neighboring nuclei, which in their turn emit new particles to react with other nuclei, thus beginning a chain-reaction which spreads through the whole mass.

Discovery of the Neutron

In 1932 Chadwick proved that, when the element beryllium was bombarded with the *alpha*-particles emitted by polonium the very penetrating radiation emitted consisted of fundamental particles which had a mass almost the same as that of a proton, but had no electric charge. These new-found particles were called "neutrons" and it was at once realized that they, together with protons, were likely to be the ultimate constituents of the nuclei of atoms of all elements. The lack of electric charge made the neutron an ideal projectile for carrying out nuclear transformations. Neutron sources could be made either by mixing radium or polonium with beryllium or by the use of an instrument, known as the "cyclotron."

In the meantime Joliot and Mme. Irene Curie-Joliot showed that certain elements, which are normally stable, undergo nuclear reactions when bombarded by *alpha*-rays and yield new atomic nuclei which are isotopes of known elements but which are not stable and decay in the way characteristic of the natural radio-active elements. In 1934 E. Fermi studied the reactions produced when the nuclei of all atomic species were subjected to neutron bombardment. The heaviest known elements were examined, particularly uranium, which was subjected to neutron bombardment. New isotopes were formed which were unstable and were subject to radio-active decay. It therefore seemed that, by bombardment of the heaviest known atom with neutrons, it was possible to produce in the laboratory atoms of higher number, 93 and upwards, than were found in nature.

Prof. O Hahn and Dr. Strassmann in Berlin, in January 1939, reported chemical evidence to show that one, at least, of the new isotopes was, in fact, an isotope of barium which has an atomic number and mass not very different from half that of uranium. Immediately afterwards Dr. O. Frisch and Prof. Lise Meitner pointed out that this discovery could only mean that, when uranium was bombarded by neutrons, a nuclear reaction took place of a kind utterly

different from any so far studied, and that the uranium nucleus split into two parts of roughly equal mass. The fragments of the uranium nucleus would fly apart with great energy.

The Chain Process

In the spring of 1939 Prof. Joliot and Drs. Halban and Kowarski proved experimentally that when the fission of uranium takes place a number of free neutrons is also produced. It was recognized that not only did the fission reaction provide the large amount of energy calculated from the difference in mass of the reactants and products, but the liberation of more than one new neutron each time that a uranium nucleus underwent fission made possible the continuation of the reaction by a chain process once the initial step has been taken. Such a process would enable the reaction, in a suitable mass of uranium, to take place at an ever-increasing rate and would involve so many atoms that there would be a sensible, and, indeed, possibly an overwhelming liberation of energy.

Uranium consists for 99.3 per cent, of atoms of mass number 238, but there is also an isotope (0.7 per cent) of mass 235 and a very small proportion (0.008 per cent) of an isotope of mass 234. The first two, conveniently designated by the symbols U238 and U235 respectively, are the most important in connection with the uranium fission project. Thorium, atomic number 90 and consisting of one isotope only of atomic mass 232, behaves in the same way as U238 and fission can only be brought about when the bombarding neutrons have very high energy. Proctactinium, atomic number 91, and atomic mass 231, behaves, as regards fission, in a manner intermediate between U235 and U238.

In recent years the enormous effort expended on the solution of this problem, has been concentrated on the development of an atomic bomb. The fact was appreciated that, if the reaction was not to "run away," it was essential to make use of neutrons of very low energy in the individual steps of the chain process. A suitable "slowing-down" medium must not have any large probability of capturing a neutron and its atoms should be of as small mass as possible in order to get the maximum rate of loss of energy in the neutrons through elastic collisions. The most suitable materials to fulfil both these conditions were "heavy hydrogen" or its compound "heavy water," helium, beryllium and carbon.

Its Potentialities

At the beginning of 1940 Dr. Fisch and Prof. Peierls, Birmingham University, and Prof. Sir James Chadwick, Liverpool University, independently called attention to the possibility of producing a military weapon of unprecedented power. They pointed out that the isotope U_{235}, if it could be separated, offered great possibilities. It seemed that the amount required to make a bomb would not be very large, certainly between one and one hundred kilos, and rough calculations showed that such a bomb might be equivalent to many thousands of tons of T.N.T.

The chain reaction will develop so fully that an explosion occurs only if the quantity of U_{235} is greater than this critical amount. Quantities less than this are quite stable and perfectly safe. On the other hand, if the amount of material exceeds the critical size it is unstable and a reaction will develop and multiply itself with enormous rapidity, resulting in an explosion of unprecedented violence. Thus all that is necessary to detonate a bomb of U_{235} is to bring together two pieces each less than the critical size but which when in contact form an amount exceeding it.

In order to release an appreciable fraction of the available energy, it is necessary that the reaction should develop so rapidly that a substantial part of the material can react before the system has time to fly apart. The interval between the beginning and the end of the nuclear reaction is exceedingly brief. In this interval the mass will have expanded so much that the nuclear reaction breaks off owing to the escape of neutrons. If only 1 lb. of U_{235} is affected this release of energy will be as much as from 8000 tons of T.N.T.

SELECTED ABSTRACTS

The Relative Effectiveness of Pure Penicillins G, X and K. R. D. Coghill, A. E. Osterberg and G. R. Hazel. *Science 103,* 709 (1946). A preliminary investigation conducted on four human subjects indicated that penicillin K is so rapidly destroyed in the body that its therapeutic usefulness is to be questioned.

The penicillins used were analytically pure samples of K, G and X haxing an activity of 2,300, 1,667 and 900 units/mg., respectively, and a new penicillin designated as "No. 128" with an activity of 3,500 units/mg. Each of the four subjects received intravenously, on different days, 25,000 units of each sample. The blood levels were determined by Heilman's method against her strain of a hemolytic streptococcus. A blood level of at least 0.03 unit/ml. was maintained as follows: penicillin G, 2-2½ hours; penicillin No. 128, 1-1¼ hours; K, ½-¾ hour; X, 4-4½ hours. Penicillin X was found to prevent hemolysis at eight times the dilution at which G, K and No. 128 were capable of doing so.

In urinary excretion studies against *Staphylococcus aureus* 209 P it was found that during the first two hours following injection, the various penicillins were excreted in the following percentages: G, 83; No. 128, 58; K, 28; X, 78.

The examination of a commercial lot of penicillin by chromatographic and other methods revealed it to contain approximately 92 per cent of G and 8 per cent of K. Blood level and urinary excretion data on this sample agreed with those observed for pure penicillin G.

Comparative Evaluation of Preparations for the Prophylaxis and Treatment of Fungous Infections of Feet. M. B. Sulzberger and A. Kanof. *U. S. Naval Med. Bull. 46,* 822 (1946). Of a total of 1,152 men examined, 52 per cent had minimal evidence of infection of the feet; an additional 14 per cent who displayed clinical infection were excluded from the prophylactic series of the investigation, but were used in the therapeutic studies. As in an earlier study, the method of paired comparisons was used, *i. e.,* the simultaneous use of two different medicaments, each on one foot of the same subject.

Undecylenic powder was found to be the most effective of the preparations tested for the prophylaxis of fungous infections of the feet. This product contained zinc undecylenate (Wallace & Tiernan) 20.0, talc 76.0, undecylenic acid (Grade AA) 2.0, and dibenzo-thio-indigo (red) 2.0.

No significant difference in efficacy between undecylenic powder and undecylenic ointment could be observed in the treatment of mild to moderate infections of the feet. The composition of the ointment was as follows: undecylenic acid (grade AA) 5.0, triethanolamine 3.0, zinc undecylenate 18.0, propylene glycol 10.0, "Carbowax 1500" 19.0, "Carbowax 4000" 29.6, distilled water 15.0, and dibenzo-thio-indigo (red) 0.4.

In one experiment to simulate combat conditions the subjects kept their shoes and socks on continuously for seven days. Undecylenic powder appeared to be more efficacious than diodoquin powder in both prophylaxis and treatment in this test. The latter preparation contained 5 per cent "Diodoquin" (Searle) in talc.

Other preparations used in this investigation included: (a) "Sopronol Powder" (Mycoloid Laboratories, Inc.), composed of calcium propionate 15.0, zinc propionate 5.0, polychloro-copper-phthalocyanine (green) 0.5, and talc 79.5; (b) vioform powder, containing either 1 or 3 per cent "Vioform" (Ciba) in talc; (c) 5 per cent thiourea in talc.

As controls, both talc (U. S. P.) and Foot Powder U. S. N. (general issue) were used. The latter contains sodium bicarbonate 10.0, sodium borate 5.0, kaolin 35.0, talc 38.0, sodium perborate 10.0, titanium dioxide 1.0, chlorothymol 0.5, and methyl salicylate 0.5.

The Present Status of Varicose Vein Sclerosing Agents. I. H. Pratt and T. D. Whittet. *Pharm. J. 102, 272* (1946). The occurrence and nature of varicose veins and the indications and contra-indications for the injection treatment are briefly discussed. The authors review the status of the following sclerosing agents:

Sodium Morrhuate. The formula for this preparation contained in the Fourth Addendum to the B. P. contains 5 per cent of sodium morrhuate, 1 per cent of ethyl alcohol and 0.1 per cent of chlorocresol. The replacement of ethyl alcohol by benzyl alcohol and buffering to pH 9.6 for maximum stability have been suggested.

Although this preparation is less likely than some of the other types to cause an injection ulcer, it has the disadvantage of sometimes causing anaphylactic symptoms. Urticarial collapse and even death may occur. It is more popular in the United States than in England.

Quinine and Urethane. This preparation is also recognized by the B. P. Fourth Addendum. It is quite stable, but may deposit crystals on standing. Patients with an idiosyncrasy to quinine may exhibit symptoms of cinchonism.

Lithocaine. A suitable formula contains procaine hydrochloride 1.0 Gm., lithium salicylate 30.0 Gm., chlorocresol 0.2 Gm., distilled water q.s. to 100.0 mils. It is sterilized by heating at 98-100° C. for 30 minutes.

It is stated to be suitable for large, deeply seated veins; up to 5 mils may be injected.

Monoethanolamine Oleate. Preparations of this type contain 5 per cent of this drug, with 25 per cent of glycerin or 2 per cent of benzyl alcohol. One proprietary brand contains monoethanolamine morrhuate instead of the oleate.

Monoethanolamine oleate is generally considered the safest sclerosing agent. Although collapse and death have followed its use, these complications are very rare. It is suitable for the smaller and more superficial veins.

Combined Injection of Lithocaine and Quinine and Urethane. This double treatment is used for treating large cavernous veins, reportedly with satisfactory results. Lithocaine is first administered and then, without removing the needle, quinine and urethane injection is also given. A precipitate forms which remains in the venous cavity.

Dextrose. Solutions containing from 56 to 60 per cent of dextrose, or 50 per cent of dextrose with 30 per cent of sodium chloride, have been recommended by some investigators. It has been stated, however, that of the recorded cases of pulmonary embolism resulting from the injection treatment for varicose veins, the majority have occurred with dextrose.

Sodium Chloride. A 20 per cent solution of sodium chloride, usually with an anesthetic, has been used. Opinion varies as to its efficacy. Cramp-like pains are said to follow its injection.

Phenol. This is seldom used at the present. From two to four minims of undiluted liquefied phenol were injected, and it has been claimed that the treatment is practically painless.

Sodium Salicylate. Solutions containing 20, 30 or 40 per cent of this compound were once used. Owing to the disadvantage of causing intense pain of several minutes' duration, coupled with the fact that if obliteration does not occur rapidly a tolerance toward the drug is established, this treatment is now seldom used.

Note on the Stability of Adrenalin Solutions. G. B. West. *Pharm. J. 102,* 251 (1946). Studies of the stability of adrenalin solutions were made, employing the isolated perfused frog heart as a means of determining the activity of the drug.

The *l*-isomer of adrenalin has about 17 times the activity of the *d*-form, a characteristic which is the property of the molecule and its configuration.

It is well known that adrenalin solutions are quite unstable, particularly in the presence of alkali. The pink color seen as the first color change may indicate the production of the corresponding quinone; if only slightly pink, the solution retains its full potency, but a deeper pink product shows a loss of 10 per cent. The addition of a trace of sodium or potassium metabisulfite to a pink solution decolorizes it and restores its full activity, probably because of reduction of the quinone.

Further decomposition of the drug yields a red color, probably due to some adrenochrome. An orange-brown color then develops; if light in color, a 15 per cent loss in activity is indicated. A light-brown solution exhibits a loss of up to 20 per cent. Only a partial recovery of potency is possible by the addition of a trace of metabisulfite to an orange-brown solution. It is possible that any adrenochrome formed is reduced to a physiologically inactive leuco-base.

The final stage of decomposition is the appearance of a black precipitate of melanin.

The addition of 0.1 per cent potassium metabisulfite to the B. P. adrenalin solution was found to aid its stability greatly.

A solution of adrenalin acid tartrate containing 0.1 per cent of metabisulfite was found to have a pH of 3.6. This solution under-

went only negligible loss of activity on autoclaving if packaged in ampuls.

The author suggests as a replacement for the present B. P. adrenalin solution the following:

(1) Solution of Adrenalin—a non-sterile preparation, and not necessarily isotonic; it should contain 0.1 per cent metabisulfite, and probably an antiseptic such as 0.1 per cent chlorocresol.

(2) Injection of Adrenalin—a sterile preparation intended for parenteral administration, and capable of withstanding autoclaving. Autoclaved preparations containing adrenalin acid tartrate, metabisulfite, sodium chloride and an antiseptic were found to retain their full activity for over twelve months.

Studies on rats, mice and frogs indicated that autoclaved adrenalin solutions in ampuls containing minute amounts of metabisulfite had practically the same toxicity as adrenalin itself.

Fluorine and Dental Caries. P. Jay. *J. A. D. A. 33,* 489 (1946). The author reviews the literature on the inverse relation which exists between the fluoride content of drinking water and the incidence of dental caries in the permanent teeth of children. Thirty-two references are cited.

The available evidence indicates that fluorine is the caries-inhibitory factor in the water supplies of communities which were found to have low dental caries rates (defined as the number of permanent teeth with caries experience per hundred children 12 to 14 years old). No correlation has been observed between the prevalence of dental caries and the mineral content of water as measured by its total hardness. Thus, the caries rate for Colorado Springs, Elmhurst (Ill.) and Middletown (Ohio) were 246, 252, and 703, respectively; the respective fluorine contents of the water supplies were 2.6, 1.8, and 0.2 p.p.m. The total hardness of the Colorado Springs water was 27 p.p.m.; that of Middletown water, 323 p.p.m.

In two long-term studies the drinking water of Newburg (N. Y.) and Grand Rapids (Mich.) is being treated with sodium fluoride to represent approximately 1 p.p.m. of fluorine, which is believed to be the optimum concentration.

It has been noted that the teeth of persons resident for the first eight years of life in areas where the drinking water contains fluorine contain more of this element than do those of persons in fluoride-free areas, and that *Lactobacilli* do not flourish in the mouths of the former. The manner in which fluorine thus apparently inhibits oral *Lactobacilli* is not understood. Experimental data on rats suggest that fluorine must come directly into contact with the bacterial flora of the mouth in order to prevent caries activity.

The Storage of Penicillin Preparations. K. Winterbottom. *Pharm. J. 102,* 366 (1946). The deterioration of penicillin ointment, solutions and lozenges on storage was studied under various conditions of temperature, *viz.,* 0°-4° C., 15° C., and 25° C.

The ointment contained 170 units of penicillin per gram and had a pH of 6.80. The loss of strength on storage at 0°-4° C. was as follows: 2 weeks, 25-30 per cent; 1 month, 30-35 per cent; 3 months, 65-70 per cent. It deteriorated much more rapidly at the higher temperatures.

In order to obtain some indication of the rate at which penicillin in ointments is destroyed when applied to the body, samples of the ointment were spread on open glass trays exposed to room temperature. No loss in potency was observed after either 6 or 12 hours, and only 5-10 per cent loss was noted after 24 hours.

Sterile solutions of calcium penicillin were prepared in two concentrations: (1) 2700 units per mil, pH 6.2; (2) 270 units per mil, pH 6.5. In the case of the diluted solution, no loss in potency was observed in samples stored at 0°-4° C. for as long as 2 months. At 15° C., no loss occurred during one week, but an 11 per cent loss was observed after 2 weeks. At 25° C., there was no loss during one week.

The concentrated solution was found to be far less capable of withstanding storage. At 0°-4° C., the losses after 2 weeks and one month were 9 and 37 per cent, respectively. At the higher temperatures deterioration occurred much more rapidly.

The base of the lozenges consisted of glucose with 8 per cent of acacia. The product, which had an initial strength of 275 units per gram, was prepared under aseptic conditions and was packaged in

sterile, corked glass tubes. At 0°-4° C. no loss occurred after storage for 2 weeks, but losses of 30-35 per cent and 55-60 per cent were noted after 4 weeks and 2 months, respectively. The loss of potency after 2 weeks was 80-85 per cent at 15° C., and 100 per cent at 25° C.

Discoloration of Solution of Eserine Sulfate. J. Rae. *Pharm. J. 102,* 329 (1946). The author reports an investigation conducted in an attempt to learn the cause of the pink discoloration which soon appears in solutions of eserine salts, and how to prevent it.

The solutions were stored in partially filled, clear flint bottles stoppered with corks, chosen as representing adverse conditions of storage. Exposure to daylight, but not to direct sunlight, was permitted.

A stock solution of eserine sulfate was diluted with solutions of the reagents chosen for the test, resulting in a 1 per cent solution of the alkaloidal salt. Storage in the dark failed to prevent discoloration in an aqueous solution. A sample containing approximately 3 per cent of boric acid developed a slight color after six days, as did another sample containing about 0.03 per cent hydrochloric acid. Solutions of eserine sulfate were found to be very sensitive toward traces of iron, caustic alkali, ammonia, and hydrogen peroxide.

A solution containing approximately 0.1 per cent of potassium metabisulfite remained colorless after nine months' storage. It is uncertain, however, whether this solution is too acid in reaction for use as eye drops.

A Case of Polyneuritis Due to Gold. E. J. R. Leiper, *Brit. Med. J.* No. 4464, 119 (1946). The case described is that of a woman of fifty-two, suffering from early rheumatoid arthritis. Treatment consisted of physiotherapy and a course of thirteen injections of 0.2 g. of myocrisin (sodium aurothiomalate). The first three injections were given weekly and the remaining ten at five day intervals. The

patient's condition improved considerably, but towards the end of the course a soreness of the mouth and, later, weakness of the legs developed. This condition spread to the arms, becoming progressively worse till the patient, bed-ridden, was unable even to sit up or turn around. There was no pain except in the fingertips.

Examination by the author seven weeks after the last injection of myocrisin showed the patient to be suffering from polyneuritis. There was symmetrical flaccid paresis of all four limbs. Many of the reflexes were absent. The sensory nervous system was much less disturbed than the motor system.

Treatment included bed rest, prevention of deformity, large doses of yeast, and later, massage. The patient improved spontaneously but very slowly, fourteen weeks elapsing before complete recovery.

In over eleven per cent of all cases of gold poisoning, neurological disorders are produced. Either the central or peripheral nervous systems may be affected. These toxic reactions assume a great variety of forms, most of them serious. However, complete recovery generally occurs, though the length of illness varies from a few days to months.

Toxic reactions occur in a high proportion of cases undergoing gold therapy. Since there is no specific treatment for this form of poisoning, prophylaxis is very important. Various authorities have held that a total of one grain of aurothiomalate, administered in weekly injections, constitutes an adequate course of treatment.

By these standards the treatment applied in the case cited above was highly intensive. However, smaller doses are still no guarantee of complete safety, since individuals vary widely in their ability to tolerate gold.

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